FOOT-AND-MOUTH DISEASE - A THREAT TO THE UNITED STATES

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To be presented before the Joint Session of the Engineering, Epidemiology, Food and Nutrition and Laboratory Sections, on October 23, 1952

History

Foot-and-mouth disease, or aphthous fever, is the first animal infection proved to be caused by a filtrable virus[1]. The agent, with an estimated particle diameter of 8 to 20 millimicrons, depending on method of measurement, is classified in Bergey's Manual[2] in Genus IV, as Hostis pecoris. The three previously accepted immunologically distinct types of the virus, classified as O, A, and C by Vallée and Carre[3], appear to have been increased to six by recent researches of the British investigators, Galloway, Brooksby and Henderson[4]. The problems of etiology and prophylaxis have been further complicated by discovery of a number of sub-types, or variants, within Vallée's types O, A, and C, which are designated A, B, and C respectively in German nomenclature[5]. The virus is resistant to alcohol, ether, phenol, and chloroform but is rapidly destroyed by highly alkaline solutions (1 to 2% NaOH)[6]. Foot-and-mouth disease occurs throughout most of the world, either enzootically or epizootically, and Australia and New Zealand are the only major livestock producing countries that have entirely escaped its ravages.

The United States has experienced the disease nine times - 1870, 1880, 1884, 1902, 1908, 1914, 1924 (twice), and lastly in 1929[7]. The earlier infections were introduced with live animals imported from infected countries. Subsequent to imposition of restrictions against such imports, the disease has gained entry several times through infected animal products. The 1908 outbreak was determined by Mohler of the Bureau of Animal Industry and Rosenau of the U. S. Public Health Service[8], to have originated from an importation of

contaminated vaccinia virus from Japan. In propagating the virus in a biological establishment, foot-and-mouth disease broke out and spread from Michigan into Pennsylvania, New York and Maryland.

The most serious epizootic experienced in the United States involved 22 States and the District of Columbia between October, 1914 and May, 1916. As in 1902 and 1908, the disease was eradicated by widespread inspection, quarantine, destruction of affected and exposed animals, and disinfection of premises. In all, over 170,000 cattle, swine, sheep and goats, and a few deer, were destroyed. As would be the case today the owners of animals slaughtered were indemnified for their loss, as well as for any property necessarily damaged or destroyed in the course of disinfection. In 1924 the disease reappeared in California and it was June, 1925 before the infection was eliminated. The disease got into herds on the forest ranges and it became necessary to slaughte. more than 130,000 animals, including 22,214 deer. During this campaign, the disease also occurred in Texas, without any apparent connection with the California epizootic, and more than 30,000 animals were killed to eliminate it. Again in 1929, the disease invaded California, but this time it was discovered before it had spread appreciably. This campaign, involving only 5 affected and 28 contact premises, was successfully concluded in less than two months.

Present Status

It has now been more than 23 years since foot-and-mouth disease has occurred in the United States. Every day, however, there is danger of its introduction. Importations of cattle, sheep, swine, goats and the other susceptible cloven-footed species are prohibited, as are the fresh, chilled or frozen meats of these species, from any country classed as infected. Presently the list includes Canada to our north, and until recently Mexico to the south

was similarly classified. Shipments of the above-mentioned animals and products are permissible at this time from only the very few countries presently not classified as infected.

Foot-and-mouth disease has existed for decades throughout Europe, Asia, most of Africa, and the South American Continent. Like other epizootic viral diseases it occurs in waves of intensity. It has been so prevalent in most countries of the world which are almost continuously exposed to reinfection that elimination by slaughter has long since been abandoned. Canada, England, Mexico, Norway and the United States have been the only countries able to persis in this radical but effective means of eradication, thus avoiding the much more serious economic loss that is suffered periodically throughout most of the rest of the world.

The United States has been fortunate in its comparative geographic isolatio and in its largely self-sufficient livestock production, although it is still necessary to import large quantities of hides, wool, animal casings, glands, and other animal products, which are permitted to enter the country only under supervision for further processing. With the aid of Customs, Entomology and Plant Quarantine, and other federal agencies, the Bureau of Animal Industry must supervise and inspect international commerce, not only along the Canadian border but at all ocean and air ports as well. A patrol force of several hundred persons was maintained until recently along the Mexican border. Far flung world commerce involving modern refrigeration that tends to preserve virus, and the increasing speed of sea and air travel present constant hazards to the livestock of our country.

Even garbage from planes and ships is refused entry for livestock feed, since it may contain infected meat scraps that could introduce foot-and-mouth disease, as occurred in California and Texas in 1924, and again in California

in 1929. The task of protection is tremendous but the impact of foot-and-mouth disease here could be disastrous. Not only do farmers derive more than half of their income from livestock, but meats, milk and other dairy products are vitally important in the American diet. It has been conservatively estimated that if foot-and-mouth disease were to become established in this country as it is in many other livestock producing countries, the productivity of the susceptible species might well be reduced by 25 percent or more. Even such a great loss would be multiplied inevitably by the stringent quarantines necessary for control. It is not only the agricultural economy that suffers, since available food supplies are reduced substantially and in turn price levels rise inevitably. So the entire national economy is involved.

Not the least of the difficulties in the United States are the sporadic, enzootic or epizootic occurrences in the country of two virus-induced vesicular diseases that are clinically indistinguishable from foot-and-mouth disease. These - vesicular stomatitis and vesicular exanthema[9] - are caused by viruses distinctly different, each from the other, or from foot-and-mouth disease. While these diseases are usually milder in character than foot-and-mouth disease and there are differences in species susceptibility and in epizootic patterns, a specific diagnosis must be made in every instance in order to prevent overlooking foot-and-mouth disease. While serum-neutralization and complement fixation technics have been reasonably well worked out, practical considerations require preliminary screening of the virus on the affected premises by means of various inoculations in different species of animals. A requisite for quick eradication of foot-and-mouth disease is prompt diagnosis, in order to limit spread of the infection.

Control and elimination of communicable diseases in livestock in the United States is exceptionally complicated by rapid movements by rail and truck of

large numbers of animals for great distances. Calves born in the so-called range states are often grown on natural forage in far removed areas. Then they are likely to be moved to the Corn Belt or elsewhere for fattening after which they are reshipped to widely scattered slaughtering centers throughout the country. Breeding animals are frequently shipped from coast to coast, and many milksheds in metropolitan areas depend largely upon replacement animals originating hundreds or thousands of miles away. So that once a highly communicable disease such as foot-and-mouth becomes established it may be widely disseminated in a few days.

Modes of Spread

The commonest means of dissemination is, of course, the infected animal itself, which may shed virus even before clinical symptoms are apparent. The virus is present in titers of 10^{-6} or higher in the coverings and fluid contents of the vesicles which form in the mouth, gastro-intestinal canal, feet, teats, and sometimes elsewhere in the skin and mucosa. During the febrile stage of the disease, virus is present in the blood and organs and in the secretions and excretions. The feeding of infected or contaminated materials or contact therewith readily reproduce the disease. Dogs, cats and horses, which are essentially resistant, may also carry the virus. Saliva, milk, urine or feces contaminate the animal's surroundings and the relatively resistant virus may be carried mechanically on feed, litter, vehicles, utensils and clothing or person of attendants.

Carcasses of animals slaughtered in the febrile stage are highly infective, especially the bone marrow, organs such as kidneys and liver, lymph nodes and residual blood, which do not undergo the lowering of pH which accompanies rigor mortis in the muscle. Trimmings of such carcasses, even though they have been chilled or frozen for months, are a common source of the disease especially for

swine in countries where such importations are allowed and garbage is fed without processing. Other animal diseases that may be so propagated include hog cholera, trichiniasis, vesicular exanthema and tuberculosis. Although home kitchen and restaurant wastes provide large quantities of nutritious, economic feed for swine and such feeding is often quite profitable, the disease problems inherent in feeding uncooked garbage are such that the practice should be prohibited.

There is some epizootiological evidence to indicate that some apparently recovered animals may serve as carriers and shedders of the virus. On the other hand, controlled experimental evidence is very meager.

People who have handled infected animals may carry the virus on their persons or clothing if these are not decontaminated. Contaminated milk cans, hay, feed bags, trucks and other farm equipment and materials are also common vehicles. Wild rats have been artificially infected and these as well as other animals may convey the virus mechanically. Numerous species of birds have been found resistant and the feces of species fed with huge quantities of virus apparently lose their infectivity within a few days. The European hedgehog may be infected either natually or artificially. In this species the disease is largely self limiting because of its lethality.

The most commonly used experimental animal is the guinea pig which may be infected readily by intradermic inoculation of the foot pads. Viremia and secondary lesions occur in this species, as in cattle, but infection is not acquired by contact. Recently it has been found at the Pirbright Institute in England that suckling white mice are highly susceptible to intra-abdominal injections of virus, which causes spastic paralysis and myositis resembling those resulting from similar injections of Coxsackie viruses(10). Generally

regarded as non-susceptible, embryonated chicken eggs have nevertheless been reported as highly susceptible to some strains of the virus intermittently passed in short series through guinea pigs and incubated eggs[11].

There is no substantial evidence to indicate that the disease is air borne. While the virus has been found in cattle fever ticks (Margaropus annulatus) that had fed on acutely affected cattle, it was not found to pass from one generation of ticks to another since the progeny from infective ticks were not found to be infective[12]. Efforts to transmit the virus by Cimex lectularius were unsuccessful, as were trials with Ixodes ricinus, while fowl ticks (Argus persicus) from which Haller's organ had been removed, are reported to have picked up virus from guinea pigs but transmission was not accomplished by feeding these ticks on other guinea pigs[13]. In essence there is little evidence, either experimental or epizootiological, that is indicative of transmission by arthropods.

Foot-and-Mouth Disease in Man

That man is highly resistant to the disease is shown by the few authenticated human cases in medical literature. Despite the repeated widespread occurrence of the disease in the United States, American literature contains not one acceptably proved case of infection in man. In the production of more than 50,000,000 doses of foot-and-mouth disease vaccine in Mexico, more than 100 persons were exposed almost daily for long periods up to as much as two years in their work involving virus suspensions containing millions of infective doses for cattle, without one even suspicious instance of infection.

Traum[14] and Olitsky[15] have reviewed the literature intensively and presented brief clinical descriptions of the very few cases of the rare, essentially mild and inconsequential human disease. Suffice it to say at this point that foot-and-mouth disease in all of its history covering more than 100 years in

many parts of the world has never become a public health problem, despite the fact that millions of people have been intimately exposed. It should be pointed out, nevertheless, that health standards could be impaired by restricted food supplies resulting from a serious epizootic in animals.

Future Prospects

There is little likelihood of foot-and-mouth disease receding for many years from its place as the number one animal disease menace in the world. The fact that the disease does not usually cause mortality in excess of 5 percent is misleading, since virulent outbreaks sometimes cause death losses up to 50 percent, extending to adult as well as young animals. There is probably no Nation, even the most backward, that would not gladly rid itself of the plague if it had the wherewithal to do so.

The disease has finally been apparently eliminated from Mexico after a cooperative effort with the United States lasting more than $5\frac{1}{2}$ years, at a direct cost to the United States government of almost $125,000,000. To continue to keep the disease out of the country will require persistent care. Nations with only land barriers, or those that find it necessary to permit importations of potentially infected animals and products have found it impossible to escape repeated inroads of the disease. In many areas, it is enzootic, recurring year after year in one type or another with greater or lesser severity It becomes necessary to resort to every possible aid in the situation, short of eradication which is generally impractical, and the danger of reinfection continues year after year. Preventive vaccines are widely used in many countries faced with the necessity of living with the disease. The utility of such products varies, depending upon the technical qualifications, authority and zeal of regulatory officials, the extent and variety of the infection and many other

factors. The aluminum-hydroxide adsorbed, formalin-inactivated vaccine developed by Schmidt[16][17] and Waldmann[18] constitutes a distinct advance in the development of weapons for combatting the disease, but this product is still deficient in many ways.

Virus for the vaccine is generally produced in cattle by intradermic inoculation of the seed virus into the mucosa of the tongue. The cattle are slaughtered at about 20 hours after inoculation or whenever the typical vesiculation has developed. The fluid and coverings of the vesicles are harvested, finely ground, homogenized, centrifugated and filtered. The resultant virus is added to a suspension of aluminum hydroxide and formalin is added. The mixture is incubated for about 48 hours to inactivate the virus. The vaccine is then tested for sterility, innocuity and potency before use.

In situations where uniformly susceptible cattle are available for production of virus and testing of the vaccine no great difficulties are encountered. But when appropriate cattle are not available in quantities, such problems as lowered virus yields and adequate testing of the vaccine become serious complications. Accordingly, efforts have been made to develop other means of propagating the virus. Frenkel[19] has succeeded in developing his technic of cultivation in the laboratory, utilizing minced tongue epithelium from normal slaughtered cattle in a synthetic nutrient fluid medium, to the point where practically all vaccine used in Holland is made with culture virus. Difficulties are sometimes encountered, however, in promptly obtaining virus of a particular strain in sufficiently high titer. Nevertheless Frenkel's technic promises to solve one of the major problems in vaccine production. Where uniformly susceptible cattle are not regularly available for testing of the product, it sometimes becomes necessary to import animals for the purpose from non-infected countries.

The United States must continue its vigilance and be in readiness to discover and combat the plague if it should again appear here. To assit in this preparation, it is expected that facilities for safe, scientific investigations in this country will be available on Plum Island in Long Island Sound, New York, and will be completed for use sometime in 1954. The Congress has appropriated funds for the purpose and plans are being developed at this time.

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